REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 1-34 are in the case.

I. ALLOWED SUBJECT MATTER

It is noted, with appreciation, that claims 1-34 are allowed. Those claims have been amended to correct minor errors and to improve their form. No new matter is entered.

II. CLAIMS 35 AND 36

Claims 35 and 36 have rejected for the reasons stated in the Action. In response, and without conceding to the rejections, claims 35 and 36 have been canceled without prejudice. Withdrawal of all outstanding rejections is respectfully requested.

III. AMENDMENTS

The specification has been amended to include customary headings, including a brief description of the drawings. A new Abstract is presented on a separate sheet attached to this response, which more closely conforms to claim 1. No new matter is entered.

IV. INFORMATION DISCLOSURE STATEMENT

An Information Disclosure Statement is submitted with the present response. The following comments are offered.

Levin *et al*. Biochem. J. (2002) *365*, 489-496 discloses that arachidonic acid is the precursor for 2 series prostaglandins and that dihomo-γ-linolenic acid is the precursor for anti-inflammatory 1 series prostaglandins. It further states that there is substantial evidence to suggest that overproduction of arachidonic acid-derived eicosanoids, but not dihomo-γ-linolenic acid -derived eicosanoids, may play a detrimental role in atherothrombotic, inflammatory and autoimmune diseases: these two n-6 fatty acids leading to distinct effects (see page 489, Introduction, column 1 line 7 to page 490, column 1, line 34). γ-Linolenic acid is described to be a precursor of both but to be metabolized first to dihomo-γ-linolenic acid.

The abstract of Levin *et al*. states that:

Prostaglandin (PG) E_1 has been shown to possess anti-inflammatory properties and to modulate vascular reactivity. These activities are sometimes distinct from those of PGE_2, suggesting that endogenously produced PGE_1 may have some beneficial therapeutic effects compared with PGE_2. Increasing the endogenous formation of PGE_1 requires optimization of two separate processes, namely, enrichment of cellular lipids with dihomo-γ-linolenic acid (20:3 *n*-6; DGLA) and effective cyclo-oxygenase-dependent oxygenation of substrate DGLA relative to arachidonic acid (AA; 20:4 *n*-6). DGLA and AA had similar affinities (K_m values) and maximal reaction rates (V_{max}) for cyclo-oxygenase-2 (COX-2), whereas AA was metabolized preferentially by cyclo-oxygenase-1 (COX-1). To overcome the kinetic preference of COX-1 for AA, CP-24879, a mixed Δ^5/Δ^6 desaturase inhibitor, was used to enhance preferential accumulation of DGLA over AA in cells cultured in the presence of precursor γ-linolenic acid (18:3 *n*-6). This protocol was tested in two cell lines and both yielded a DGLA/AA ratio of approx. 2.8 in the total cellular lipids. From the enzyme kinetic data, it was calculated that this ratio should offset the preference of COX-1 for AA over DGLA. PGE_1 synthesis in the DGLA-enriched cells was increased concurrent with a decline in PGE_2 formation. Nevertheless, PGE_1 synthesis was still substantially lower than that of PGE_2. It appears that employing a dietary or a combined dietary/pharmacological paradigm to augment the cellular ratio of DGLA/AA is not an effective route to enhance endogenous synthesis of PGE_1 over PGE_2, at least in cells/tissues where COX-1 predominates over COX-2.

Thus, Levin clearly discloses that diet or pharmacological administration of γ-linolenic acid or dihomo-γ-linolenic acid is not likely to be effective in treating inflammatory states.

Fisher and Harbige: Biochemical Society Transactions (1997) 25 343S discloses that feeding high doses of Borage oil, rich in γ-linolenic acid residues, did not alter LPS induced TNF-α production from PBMCs. Furthermore, Fisher and Harbige disclose that the Borage oil did increase TGF-β1, but that this is not necessarily a good thing as systemic administration of TGF- β1 had been shown exacerbate certain inflammatory conditions, predisposing to some infections.

Wahl S M ((1994) The Journal of Experimental Medicine, Vol. 180. 1587-1590 (referred to by Fisher and Harbige) discloses that TGF-β1 had different effects when administered systemically as opposed to locally and is capable of both 'good' and 'bad' outcomes.

This prior art thus discloses that Borage oil of unspecified composition could elevate TGF-β1 levels in healthy volunteers, but the consequences of this for any disease state are uncertain. Effect on TNF-α was not seen unlike with fish oil.

The presently claimed invention specifies parameters of a method of treating Multiple Sclerosis by administration of a Borage oil of particular composition wherein TGF-β1 is elevated and the TNF-α level decreased which resulted in surprisingly beneficial effect for patients.

The Examiner is requested to initial and enter the IDS and to return a copy of the initialed document to the undersigned with the next paper to issue in this case.

Favorable action is awaited.

Respectfully submitted,

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